DARPA Biological Warfare Defense Program

Program Overview

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Why Is Biological Warfare Defense a Very High DARPA Priority?

- Troops, ports, airfields, supply depots, etc., are vulnerable to biological attacks
- A number of countries have developed or are developing offensive biological capability
- Most likely first use will be against population centers of ours or our allies
- Small demonstration and threat are probably adequate to immobilize national will with panic unless reasonable defenses are available

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New Threats From Advances in Bioengineering

- Bioengineering technology is becoming more widespread and accessible to non-experts
- Bioengineering means possibly new, previously unseen pathogens
- Terrorists do not need the technological sophistication of a military offensive BW program

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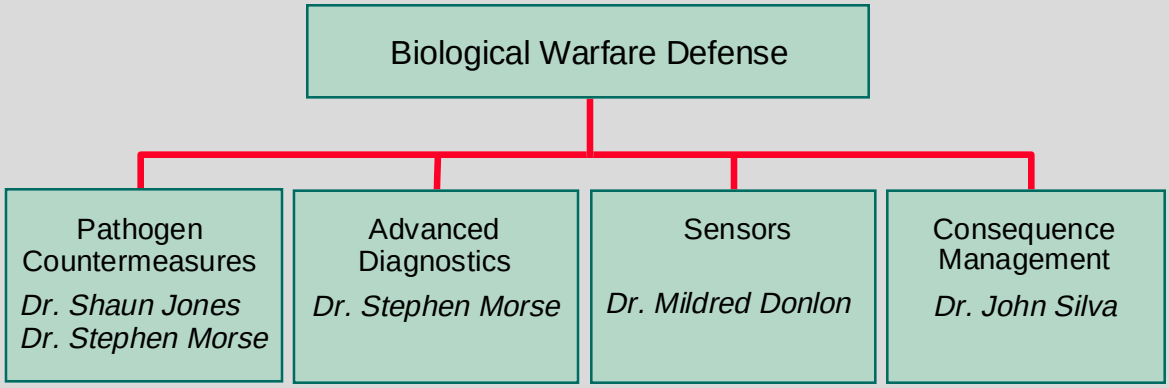
DARPA Biological Warfare Defense Program



Goal: Remove the threat of biological warfare agents (including bacterial, viral, and bioengineered organisms) as a factor in the planning and conduct of U.S. military operations

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Time Scales for Development

- Consequence Management
  - Prototyping with users now
  - This program thrust ends in FY99
- Sensors
  - Developing technologies to transition to prototyping in 3-5 years
  - Tissue-based sensors fieldable in 5-10 years
- Advanced Diagnostics
  - Thrust 1 diagnostic prototypes in 2-5 years
  - Thrust 2 develops diagnostics to match Pathogen Countermeasures developments
- Pathogen Countermeasures
  - Developing revolutionary new approaches, available in 8-12 years

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Biosensor Program Objectives

	Size/ Weight	Cost	Sensors	False Alarms	Automation	Time
Current	Large/ 20-60 lb	Moderate $70-150K	Single	Low False Alarms	Man-in-Loop	17 min
DARPA	Tiny/ < 5 lb	Low-Cost < $5K	Integrated, Multi-Agent; Dead vs. Live	No False Negatives, Few False Positives	Unattended	< 2 min

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Shifting the Paradigm of Biodetection Technology

Technology	Advantages
Direct Gene Identification	■ Detects single gene without PCR amplification ■ Uses bacterial RNA (10^5-10^8 copies/cell) for identification of species, virulence factors, and viability within minutes
Upconverting Phosphors (UCP)/ Giant Magnetoresistance (GMR) Readout	■ Eliminates amplification - able to read single bead (single agent, single gene) ■ Dramatically increases sensitivity and decreases detection time. UCP/GMR adapts well to chip technology
Structure Based Drug Design/Combinatorial Chemistry	■ Replaces antibody in sensors with designer molecules ■ Enables aerogels containing designer molecules for agent capture

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Shifting the Paradigm of Biodetection Technology (Cont.)

Technology	Advantages
MS/MS: Miniaturized	■ Small biodetector as unattended sensor - no fluids required
Developmental Technologies	■ Determines live vs. dead spores, and pathogenic vs. non-pathogenic bacteria ■ Embeds antibodies and receptors in polymeric materials

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Tissue Based Biosensor for BW/CW Detection

Goal: Develop multifunctional physiological bioassay system(s) utilizing singular and multicellular arrays to provide early warning for chem/bio agents: toxins, nerve agents, bioregulators and other chemicals

Figures of Merit

- Detect both known and previously uncharacterized agents affecting human performance
- Determine physiologically active vs. inactive agents
- Mimic complex multicellular human tissue function
- Small, compact, and robust

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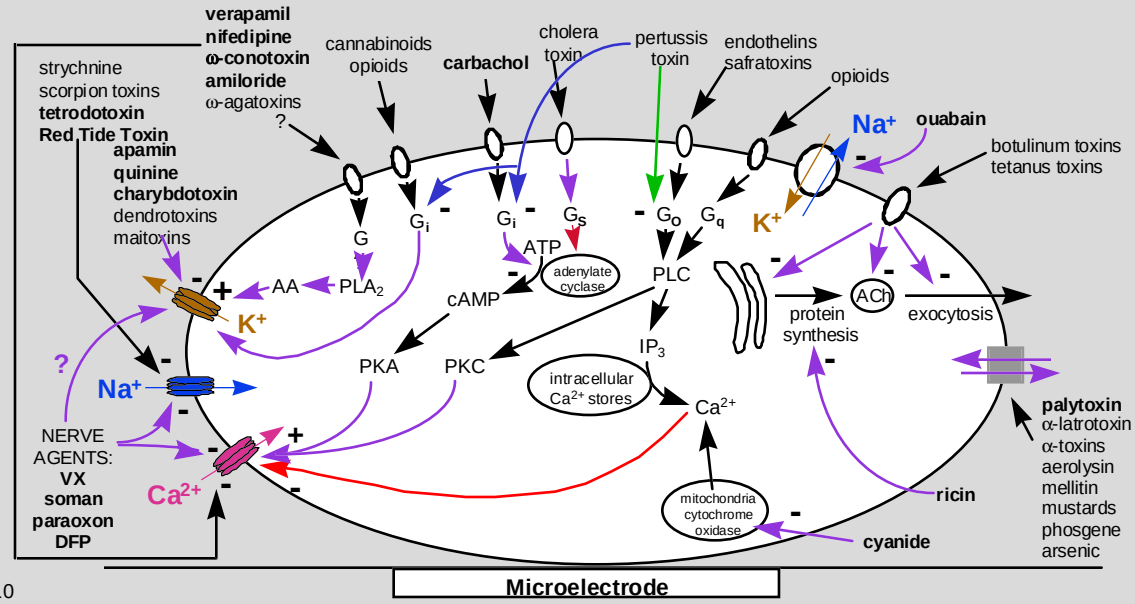
Nerve Cell CBW Inhibition Pathways

All Known Toxin Pathways Lead to Attenuation of Electrochemical Activity



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Impact of Tissue Based Sensors

- Activity (physiology) based biosensor
  - No current capability for the detection of *uncharacterized* BW/CW agents
- Early warning for BW/CW standard operating procedures
- Assessment of decontamination and neutralization activities
- Indications for medical treatments
  - Exposure level
  - Mechanisms of action

Information Problems

- Managing the consequences of a BW attack is *very* complex, requiring knowledge not usually available in real-time
- Lack of access to the “few who know”
- Information flood can overload user; needs to be cogent or organized to meet the need
- Course of action is not well known or structured; correct protocols needed

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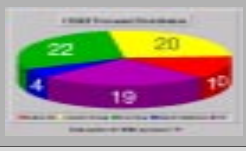
Biological Warfare Defense Anchor Desk Situation Display

- Purpose
  - Provide an up-to-date electronic watchboard
  - Distribute and display data to Command Operations Center and reachback team
- Approach
  - Monitor the flow of casualties
  - Display geographic locations
- Benefit
  - Accelerate management of a BW incident
  - Enhance situational awareness

Watch Officer	Wind Direction	Weather Data	Contamination Hazard	MOPP Level
Maj. Malone	45	A. WBTG 5.5 B. Wind Speed (km/hr) 10 C. Flag Condition		A. MOPP 0 X B. MOPP I C. MOPP II D. MOPP III E. MOPP IV F. Level A
Checklist	**Comm Plan**	**Call Signs And Freq.**	**Other Agencies On Scene**	**CBIRF Personnel By Zone**
28. All Casualty Clearing Out of Incident Site Code: Padress From: Hot Zone Coordinator To: S3 Time: 1		CO Centurion CoC CBIRF S3 Moses SCT Hornet Medical Stingray Recon Viper SSE Rucksack Decon Ajax Security PittBull		A. Hot Zone 0 B. Warm Zone 0 C. Cold Zone 0
Casualty Estimation By Type	**Patients Processed By Type**	**CBIRF Casualties**		
Type 0 0 Type I 0 Type II 0 Type III 0	Type 0 0 Type I 0 Type II 0 Type III 0	A. Chem/Bio Wounded 0 B. Chem/Bio Deaths 0 C. Cvntl Wounded 0 D. Cvntl Deaths 0 E. Medevaced 0		



Operational Impact of BWD Informatics

- Medical protocols down to appropriate echelon of care for correct diagnosis and treatment
- Reachback to experts and useful information
- Identification of BW attack from scattered illness reports
- Readiness information to military commanders of present and projected BWD casualties
- Tie into logistics to get needed treatment/supplies
- Effective BWD training tools for medical personnel

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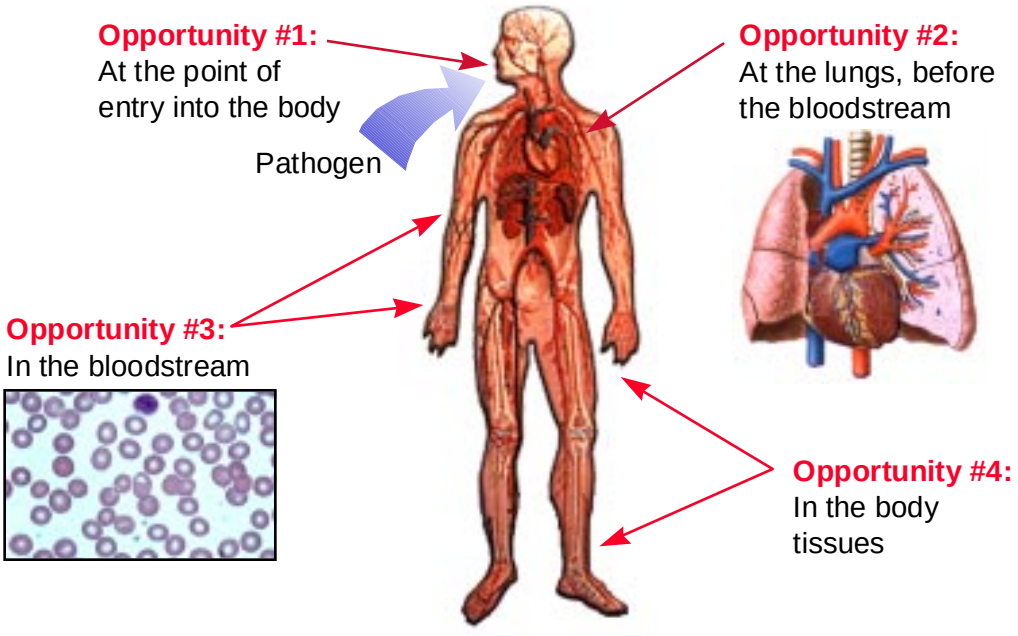
Defense Against Pathogen Attack: A Multi-Level Approach



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Medical Countermeasures: Program Goals

- Defeat a pathogen's ability to enter the body and reach target tissues
- Target common mechanisms of pathogenesis and functions or structures shared by groups of pathogens
- Modulate the human biological response to pathogens

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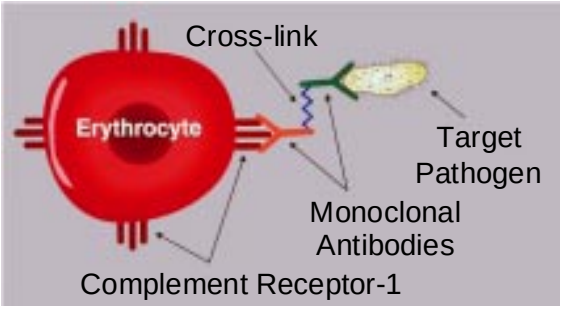
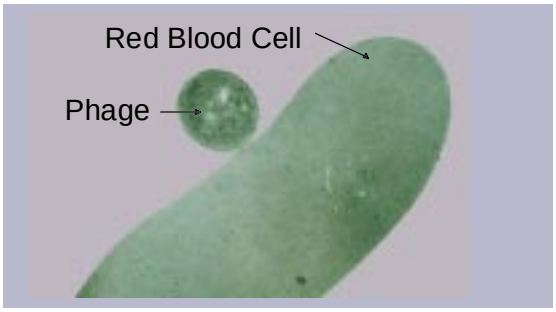
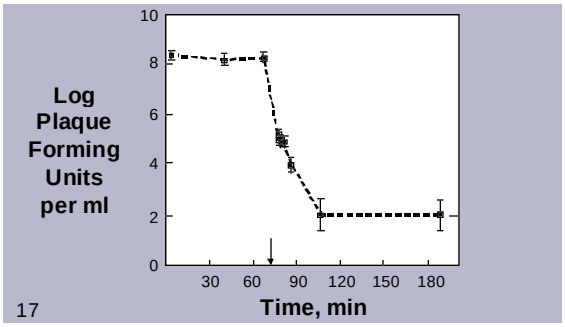
Heteropolymer Mediated Binding of a Target Pathogen to Red Blood Cells







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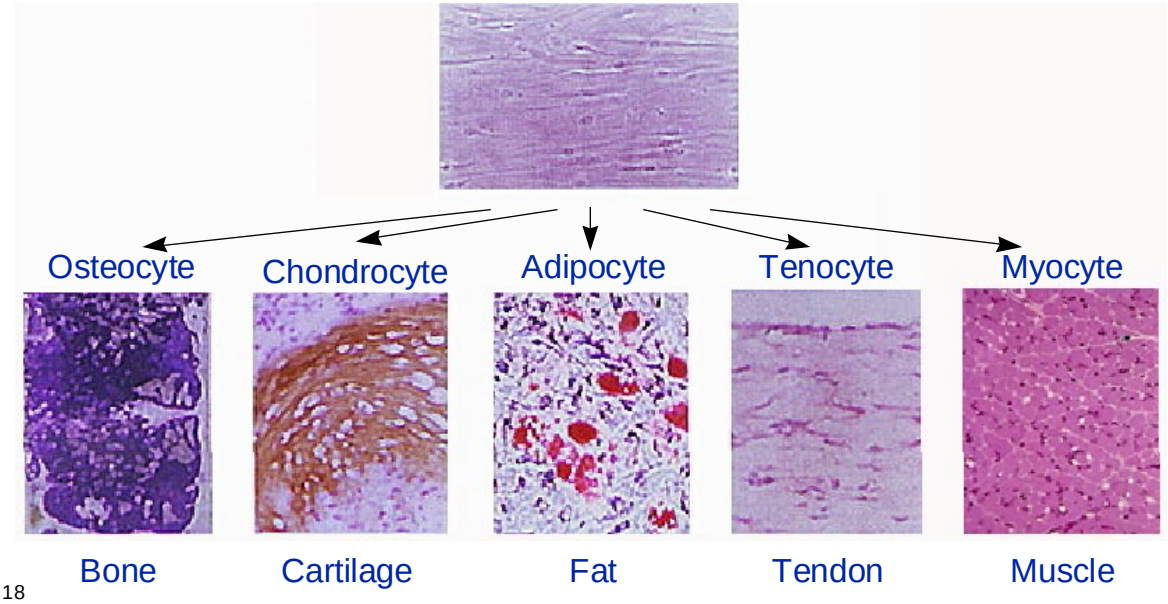
Conclusions and Implications

- Demonstrated greater than 1 million fold reduction of virus from bloodstream in 1 hour
- Bound heteropolymers have a >2 day lifetime in the circulation and may be useful for short-term passive immunization
- Early experiments show no toxicity and minimal immunogenicity

Mesenchymal Stem Cell Differentiation



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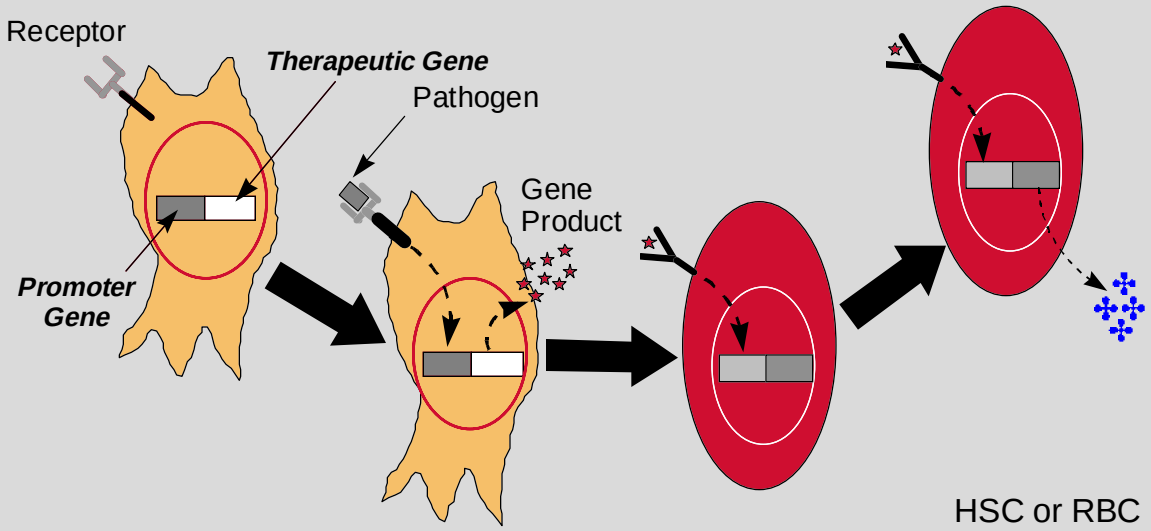
Modified Mesenchymal Stem Cells Detect Pathogens and Release Products



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Why Target Common Pathways?

Targeting common pathways fundamental to the infection or disease process will be:

- Effective against both known and unknown threats
- Difficult to circumvent
- Likely to be effective against bioengineered agents

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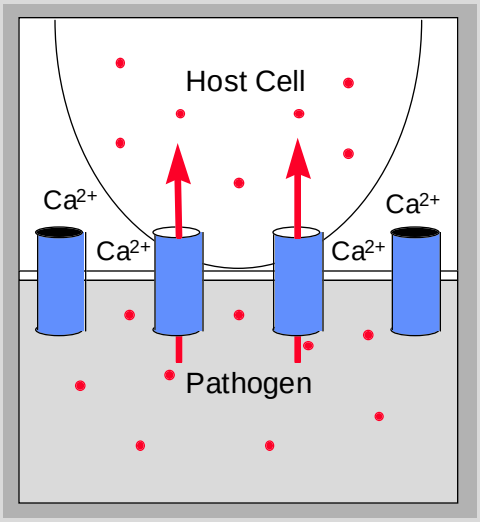
Common Pathway to Attack Broad Classes of Pathogens: An Example

Blocking the Type III Secretion System



- Type III secretion system used by many bacteria (e.g., plague, salmonella, shigella, *E. coli*)
- Pathogen - host cell contact activates virulence genes
- Virulence factors regulated by specialized secretion systems

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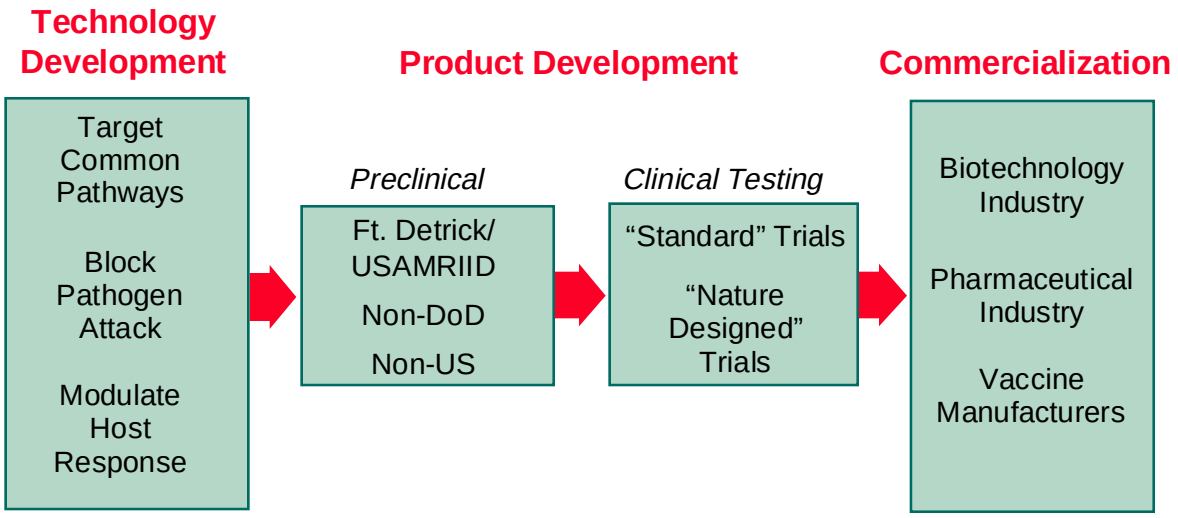
DARPA Investment in Early Phases



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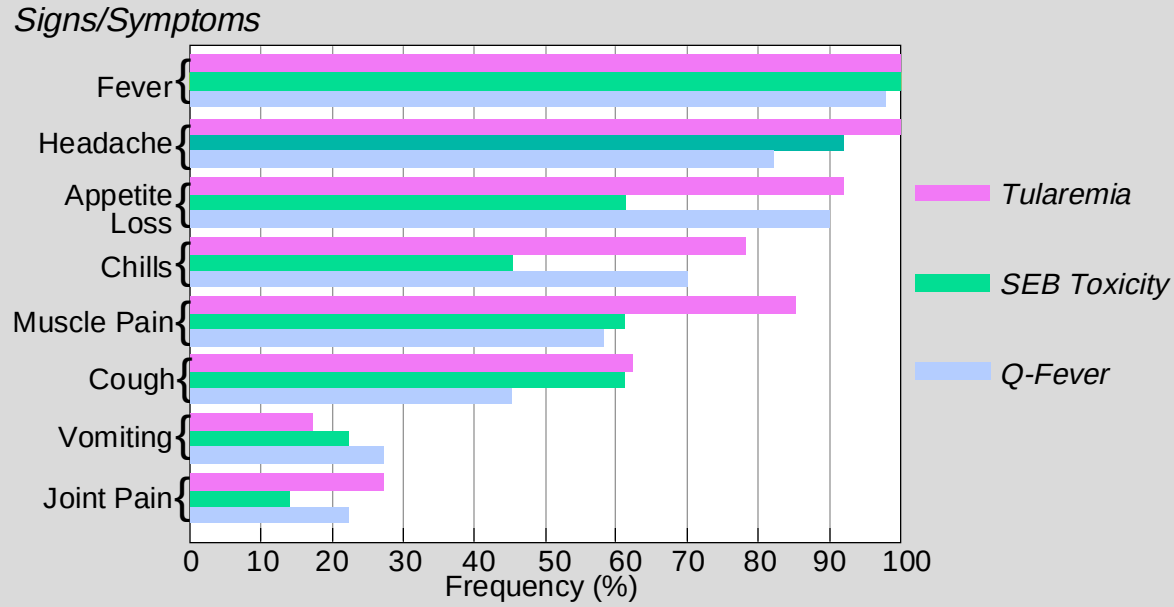
Human Response to Pathogen Exposure



23 *Early symptoms of many BW agents are flu-like and indistinguishable*

Advanced Diagnostics Program

Goal: Rapid diagnosis of infection with real-time identification of responsible organism/toxin

- Thrust 1 (multi-agent, agent specific)
  - Identify organisms rapidly from patients in early stages of infection when pathogen numbers are still low
- Thrust 2 (multi-agent, based on common virulence targets or host responses)
  - Instruments able to identify genes, products, or virulence pathways particular to pathogen classes – not agent specific

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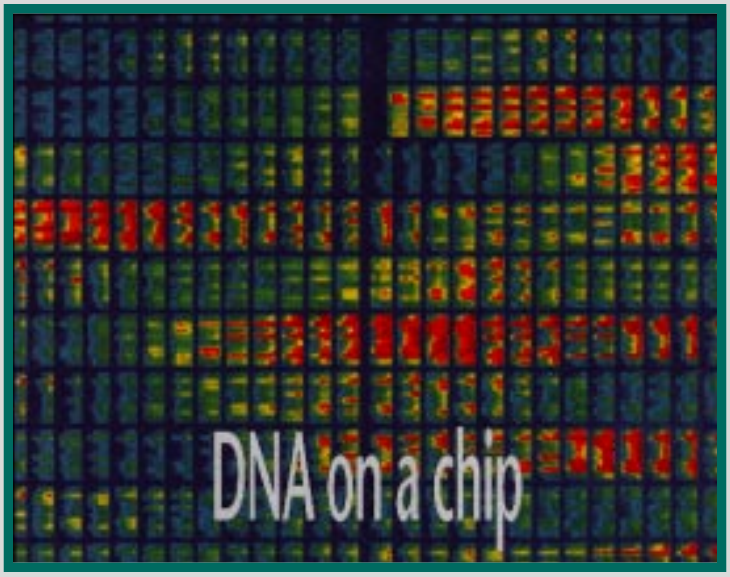
Leverage Industrial Emerging Technology in Array-Based Diagnostics



DARPA will:

- Develop and/or procure probes for known BW agents
- Develop probes for common virulence pathways
- Functionalize probes for use on BW arrays
- Demonstrate prototype instruments

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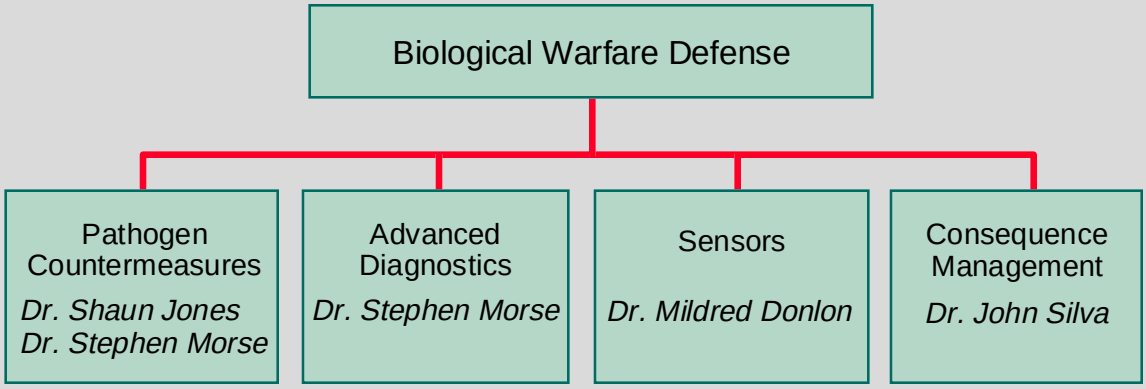

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